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Claudia Cioli[1*], Hervé Abdi[2], Derek Beaton[2], Yves Burnod[1], Salma Mesmoudi[3]

[1] Laboratoire d'Imagerie Biomédicale UMPC - INSERM U1146 - CNRS UMR 7173, Paris, F-75634, France
[2] School of Behavioral and Brain Sciences, The University of Texas at Dallas, Dallas, TX 75080-3021, USA
[3] Université Paris 1 Panthéon-Sorbonne, Equipement d'Excellence MATRICE, Paris, F-75231, France
*claudia.cioli.c@gmail.com

Abstract* — *We explore the relationships between the cortex functional organization and genetic expression. Previous work suggests that functional cortical networks (resting state, task based and anatomical) are organized as two large networks (differentiated by their preferred information processing mode) shaped like two rings. The first ring–Visual-Sensorimotor-Auditory (VSA)–process real time world interactions. The second ring–Parieto-Temporo-Frontal (PTF)–comprises networks dedicated to cognitive functions, emotions, biological needs, and internally driven rhythms. We found that the patterns of expression of the genes most differentially expressed across the cortex organized the cortex into two sets of regions that match the two rings. We found that several of the proteins–coded by genes that most differentiate the rings–were involved in neuronal information processing such as ionic channels and neurotransmitter release. The systematic study of families of genes revealed specific proteins within families preferentially expressed in each ring. The results showed strong congruence between the preferential expression of subsets of genes, temporal properties of the proteins they code, and the preferred processing modes of the rings.

Index terms* - *Genetic Imaging, Magnetic Resonance Imaging.

I. INTRODUCTION

In order to understand how the human cerebral cortex processes information we need to connect the anatomo-functional organization of the cortex with the topographic organization of gene expressions. To do so, several recent studies have analyzed–in species such as monkey, mouse, and human–the pattern of genetic expression of cortical regions (e.g., visual or prefrontal cortices). These studies revealed that cortical regions differ in the genes that they express. In humans–because the strong constraints of postmortem genome-wide analysis make the data hard to obtain–only very few studies have explored the systematic anatomic organization of genetic expression across the whole brain.

By contrast with this small number of genetic systematic analyses, there are several systematic analysis of anatomo-functional cortical networks and functional connectivity as revealed by brain imaging.

Recent work [1] suggests that functional cortical networks (resting state, task based and anatomical) are organized as two large networks shaped like rings. The first ring—called the Visual-Sensorimotor-Auditory (VSA) ring—processes real time world interactions. The second ring—called the Parieto-Temporo-Frontal (PTF)—comprises networks dedicated to higher cognitive functions, language, working memory, and memory.

In the present study [2], we explore the differential expression of genes into the two rings and the differential properties of related proteins critical for information processing. To estimate cortical genetic expression we used the Allen Human Brain Atlas (ABA see [3]) of the human transcriptome–produced by the Allen Brain Institute–which provides microarray expression profiles of almost every gene of the human genome at hundreds of locations in the brain for two complete postmortem brains.

II. MATERIALS AND METHODS

The data for two complete post-mortem brain were obtained from the Allen Human Brain Atlas project [3]. For each data set, we used only the cortical regions. The cortical regions for each subject were labeled according to their MNI coordinates as belonging to the VSA or PTF rings.

In order to describe cortical genetic organization we used correspondence analysis (CA). CA–a variant of principal

component analysis (PCA)–is used when the goal is to compare observations according to the relative distributions–as opposed to the absolute values–of a set of variables. Here, observations are brain regions and variables are genes, as measured by their expression values.

In order to test our hypothesis that the profile of genetic expression of a region depends upon its ring (i.e., VSA or PTF), we used discriminant correspondence analysis (DiCA)–a discriminant analysis version of CA –to predict the regions' ring from their gene expression profiles.

We used bootstrap resampling techniques (Bootstrap and permutation tests) to evaluate the stability and reliability of the results from both CA and DiCA.

III. RESULTS

The first dimension of CA identified two distinct subsets of cortical regions. These subsets closely match the PTF and VSA rings. The large proportion of variance explained by Dimension 1 of the CA indicates that the different profiles of genetic expression are associated with different rings.

To corroborate this result we performed DiCA and we showed that we can actually predict the ring membership of cortical regions based on their genetic profile.

Within the most differentially expressed genes we found genes coding for proteins involved in neuronal information processing such as ionic channels and neurotransmitter release. Results showed strong congruence between temporal properties of these proteins, and preferred processing modes of the rings (see Figure 1).

Ionic channels and release-related proteins more expressed in the VSA ring favor temporal precision of fast evoked neural transmission (Sodium channels SCNA1, SCNB1 potassium channel KCNA1, calcium channel CACNA2D2, Synaptotagmin SYT2, Complexin CPLX1, Synaptobrevin VAMP1). Conversely, genes expressed in the PTF ring favor slower, sustained, or rhythmic activation (Sodium channels SCNA3, SCNB3, SCN9A potassium channels KCNF1, KCNG1) and facilitate spontaneous transmitter release (calcium channel CACNA1H, Synaptotagmins SYT5, Complexin CPLX3, and synaptobrevin VAMP2).

IV. DISCUSSION – CONCLUSION

The expression of the genes most differentially expressed across the cortex organized the cortex into two sets of regions (called rings) that match two–previously described–large scale human functional cortical networks. The first ring processes real time sensory-motor information whereas the second ring processes multi-scale temporal information such as language, memory, or vital rhythms. The systematic study of families of genes coding for ionic channels and transmitter release proteins showed strong congruence between the preferential expression of genes, the temporal properties of the proteins they code at the cell level, and the temporal processing modes of these two large scale networks.

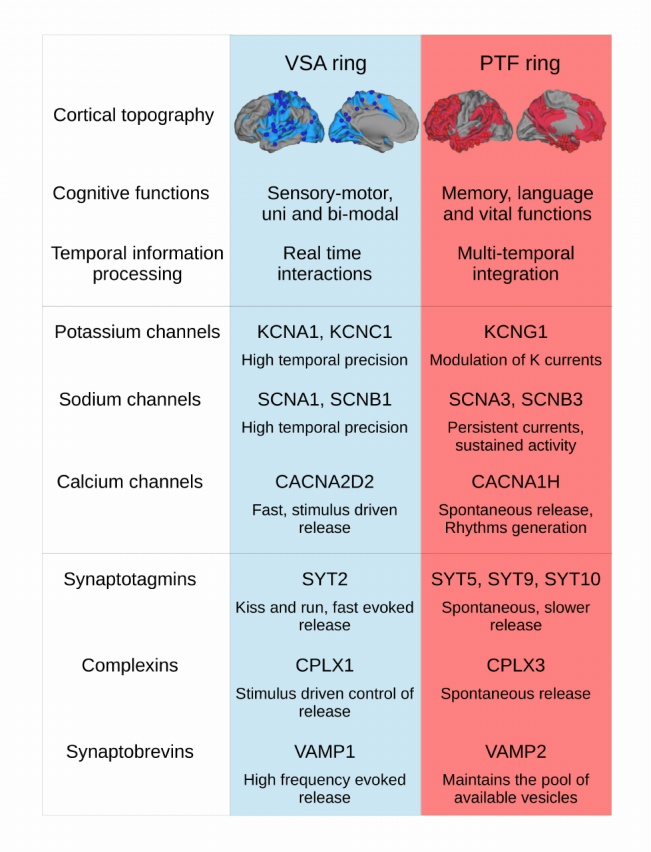

Figure 1: Proteins' temporal properties match the preferred temporal properties of VSA and PTF rings.

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